REMARKS

This amendment is responsive to the final Office Action mailed October 21, 2002. Claims 1-79 were pending in the instant Application, and Claims 1-12 were under consideration. In this amendment, Claims 1-79 are cancelled without prejudice to Applicants' right to pursue the subject matter of the cancelled claims in one or more related continuation, divisional or continuation-in-part application(s) and new Claims 80-91 are presented. Thus, following entry of the present amendment, Claims 80-91 will be pending and under consideration.

I. The Amendment to the Claims

In the present amendment, Claims 1-79 are cancelled and new Claims 80-91 are presented for examination. New Claims 80-91 are fully supported by the specification and claims of the application as originally filed.

In particular, support for new Claim 80 can be found, for example, in Claim 1 as originally filed and in the specification at page 40, lines 20-29, and at page 44, lines 10-20. Support for new Claim 81 can be found, for example, in Claim 2 as originally filed and in the specification at page 40, lines 20-29. Support for new Claim 82 can be found, for example, in Claim 3 as originally filed and in the specification at page 42, line 33 to page 43, line 2.

Support for new Claim 83 can be found, for example, in Claim 4 as originally filed and in the specification at page 40, line 31 to page 41, line 21. Support for new Claim 84 can be found, for example, in Claim 5 as originally filed. Support for new Claim 85 can be found, for example, in Claim 6 as originally filed and in the specification at page 42, line 33 to page 43, line 2.

Support for new Claim 86 can be found, for example, in Claim 7 as originally filed and in the specification at page 41, line 23 to page 42, line 11. Support for new Claim 87 can be found, for example, in Claim 8 as originally filed. Support for new Claim 88 can be found, for example, in Claim 9 as originally filed and in the specification at page 42, line 33 to page 43, line 2.

Support for new Claim 89 can be found, for example, in Claim 10 as originally filed and in the specification at page 42, lines 13-30. Support for new Claim 90 can be found, for example, in Claim 11 as originally filed and in the specification at page 164, lines 13-19. Support for new Claim 91 can be found, for example, in Claim 12 as originally filed and in the specification at page 42, line 33 to page 43, line 2.

Further support for new Claims 80, 83, 86, and 89 is provided by Claims 1, 4, 7, and 10 as amended in the amendment filed September 27, 2002. These amendments to Claims 1, 4, 7, and 10 were entered without objection in the Office Action mailed December 3, 2002, indicating that the PTO considered this amendment to be fully supported by the application as filed.

In view of the foregoing, Applicants respectfully submit that new Claims 80-91 are fully supported by the specification and claims of the application as originally filed. Accordingly, no new matter is introduced by the instant amendment. Therefore, Applicants hereby respectfully request entry of the present amendment under 37 C.F.R. § 1.116.

Applicants believe that the present amendment is suitable for entry under 37 C.F.R. § 1.116 because it places the claims in condition for allowance, because it presents the same number of claims as was previously pending, and because no new search would be required to examine the subject matter of the present claims. Accordingly, Applicants earnestly request that the present amendment be entered into the record of the present application.

II. The Provisional Rejection of Claims 1-12 under 35 U.S.C. § 101

Claims 1-12 stand rejected under 35 U.S.C. § 101 as directed to the same invention claimed by Claims 1-12 of U.S. Application No. 09/663,458 ("the '458 application"). Without acquiescing to the propriety of the rejection, Applicants respectfully submit that the rejection is moot in view of the cancellation of Claims 1-12 of the present application, and hereby request its withdrawal.

In addition, Applicants respectfully request, if the only outstanding issue regarding new Claims 80-91 is a provisional double patenting rejection under § 101, that new Claims 80-91 be passed to issuance and that any non-provisional double patenting rejection based on § 101 be made in the '458 application rather than the present application. *See* M.P.E.P. § 804 I.B.

III. The Provisional Rejection of Claims 1-12 under the Judicially-Created Doctrine of Obviousness-Type Double Patenting

Claims 1-12 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over Claims 98-112 and 114-117 of U.S. Application No. 09/766,344 ("the '344 application") in view of Patick *et al.*, 1998, *Antimicrob. Agents Chemother.* 42(10):2637-2644 ("*Patick*"). Without acquiescing to the propriety of the rejection, Applicants respectfully submit that the rejection is moot in view of the cancellation

of Claims 1-12. Further, Applicants respectfully submit that new Claims 80-91 are not obvious variants of any claim of the '344 application.

A. The Legal Standard

Under the judicially-created doctrine of obviousness-type double patenting, a claim must be patentably distinct from a claim of an already issued patent or pending application. *See General Food Corp. v. Studiengesellshaft Kohle mbH*, 23 U.S.P.Q.2d 1839 (Fed. Cir. 1992). If the claim at issue defines more than an obvious variation of the patented or pending claim, it is patentably distinct and rejection of the claim under the doctrine of obviousness-type double patenting is improper. *See id.* To establish a proper obviousness-type double patenting rejection, the Examiner must show that the claim at issue is a "mere variation" of the patented or pending claim that "would have been obvious to those of ordinary skill in the relevant art." *See In re Kaplan*, 229 U.S.P.Q. 678, 683 (Fed. Cir., 1986). Finally, where the claim at issue is alleged to be an obvious variant of a currently pending claim, a rejection on these grounds is provisional. *See* M.P.E.P. § 804 I.B. If such a provisional rejection is the last remaining issue preventing passage of the rejected claim to issuance, the rejection should be removed and the claim in the other pending application should be non-provisionally rejected. *See id.*

B. Claims 80-91 are not Obvious Variants of any Claim of the '344 Application

Claims 80, 83, 86, and 89 recite, *inter alia*, methods for assessing the effectiveness of protease anti-retroviral therapy that comprise detecting a mutation in codon 88 of HIV protease, optionally in combination with a mutation in one or more additional codons of HIV protease. These mutations affect the susceptibility of the protease to protease inhibitors, including amprenavir, nelfinavir, and indinavir.

No claim of the '344 application recites any method for assessing the effectiveness of protease anti-retroviral therapy that comprises detecting a mutation in codon 88 of HIV protease. No claim of the '344 application even remotely suggests that a mutation in codon 88 of HIV protease is relevant to any method claimed therein. The claims pending in the '344 application are directed to methods for assessing the effectiveness of protease anti-retroviral therapy that comprise detecting combinations of mutations (a mutation at codon 82 and a secondary mutation at one or more codons selected from the group consisting of 73, 55, 48, 20, 43, 53, 90, 13, 84, 23, 33, 74, 32, 39, 60, 36 and 35, or a mutation at codon 90 and a secondary mutation at one or more codons selected from the group consisting of 53, 95, 54,

84, 82, 46, 13, 74, 55, 85, 20, 72, 62, 66, 84, 48, 33, 73, 71, 64, 93, 23, 58 and 36) in HIV protease, none of which is a mutation at codon 88 that can also affect susceptibility of such enzymes to protease inhibitors. Thus, no claim of the '344 application provides any suggestion that a mutation at codon 88 should be detected in a method for assessing the effectiveness of protease anti-retroviral therapy.

Moreover, *Patick* cannot properly be combined with the '344 application to show that Claims 80-91 are obvious variants of any claim of the '344 application. As described above, *Patick* can only be used to show that one of ordinary skill in the art would view the claims of the present application as obvious variants of the claims of the '344 application. *Patick* shows no such thing. *Patick* provides no teaching or suggestion that a mutation at codon 88 contributes to the effectiveness of anti-retroviral therapy, and as such surely fails to teach or suggest that such a mutation should be substituted for the combinations of mutations at other codons in the methods recited by the claims of the '344 application.

In view of the foregoing, Applicants respectfully submit that Claims 80-91 are not obvious variants of any claim of the '344 application, and therefore Claims 80-91 should not be rejected under the judicially-created doctrine of obviousness-type double patenting.

IV. The Rejection of Claims 1-12 under 35 U.S.C. § 102(a)

Each of Claims 1-12 stands rejected under 35 U.S.C. § 102(a) as allegedly anticipated by *Patick*. In response, Applicants respectfully submit the rejection is moot in view of the cancellation of the rejected claims, and further submit that the cited references do not teach each and every element recited by new Claims 80-91. Thus, *Patick* does not anticipate new Claims 80-91.

A. The Legal Standard for Anticipation

The standard governing anticipation under 35 U.S.C. § 102 requires strict identity. *See* M.P.E.P. § 2131. Thus, "for a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." *See In re Bond*, 15 U.S.P.Q.2d 1566 (Fed. Cir., 1990). Anticipation is not shown even when the differences between the claims and the cited reference are allegedly "insubstantial" and any missing elements could be supplied by the knowledge of one skilled in the art. *See Structural Rubber Prod. Co. v. Park Rubber Co.*, 223 U.S.P.Q. 1264 (Fed. Cir., 1984). Furthermore, in *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 U.S.P.Q. 253 (Fed. Cir., 1985), the Federal Circuit explained that even if the prior art teaches "substantially the same thing" as the claimed invention, the reference still cannot anticipate

the invention. Thus, a cited reference must describe each and every claim limitation in order to anticipate the invention as claimed.

Furthermore, the single cited reference must enable one of skill in the art to practice the claimed invention in order to anticipate the claim under 35 U.S.C. § 102. This requirement mandates that "the single reference must describe and enable the claimed invention, including all claim limitations, with sufficient clarity and detail to establish that the subject matter already existed in the prior art and that its existence was recognized by persons of ordinary skill in the field." *See Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Education and Research* 64 U.S.P.Q.2d 1292 (Fed. Cir., 2002) and *Crown Operations International, Ltd. v. Solutia, Inc.* 62 U.S.P.Q.2d 1917 (Fed. Cir., 2002). In other words, "for the *invention* of [the patent at issue] to be *described* in the [allegedly anticipatory reference], pursuant to § 102, the [allegedly anticipatory reference] itself must enable someone to practice the invention of [the patent at issue]. *See Reading & Bates Construction Co. v. Baker Energy Resources Corp.* 223 U.S.P.Q. 645 (Fed. Cir., 1984) (emphasis in original). Thus, the cited reference must enable the ordinarily skilled artisan to recognize that each element of the claimed invention is described in the reference. If one of ordinary skill in the art would not recognize that each element of the claim is disclosed by the reference, then it cannot and does not anticipate the claimed invention under 35 U.S.C. § 102.

B. *Patick* does not Teach Each and Every Element of the Invention as Presently Claimed

Claims 80-91 as presented in the present amendment generally relate to methods of assessing the effectiveness of protease antiretroviral therapy in patients by detecting mutations at certain recited codons of the gene encoding HIV protease in viral nucleic acids. In particular, Claims 80-91 relate to methods for assessing the effectiveness of amprenavir, nelfinavir, and/or indinavir therapy in the treatment of HIV by detecting mutations in certain codons of HIV protease. *Patick* teaches or suggests none of these methods.

In particular, *Patick* does not teach or suggest a method for assessing the effectiveness of amprenavir therapy in an HIV-infected patient that comprises, *inter alia*, detecting the presence of a mutation in codon 88 of HIV protease. *Patick* discusses particular single and multiple HIV protease mutants isolated from patients that have undergone nelfinavir therapy. *Patick* postulates that the mutations observed in HIV protease from such patients are responsible for resistance to nelfinavir and possibly other protease inhibitors. To test this hypothesis, *Patick* constructs a variety of single, double, and multiple mutants of HIV protease and determines the EC_{90} of these various HIV proteases for nelfinavir and other

protease inhibitors. *See Patick* Tables 1 and 2. *Patick* concludes that nelfinavir resistance results from mutations at codon 30, and not from mutations in other codons, and certainly not from codon 88. *See Patick* at page 2640, last sentence of the paragraph bridging the two columns and second sentence of subsequent paragraph, and at page 2642, column 1, third full paragraph, first sentence. In fact, *Patick* concludes that single mutations at codon 88 have no significant effect on susceptibility of the mutant protease to amprenavir or any other tested protease inhibitor. *See Patick* at Figure 3. Therefore, *Patick* does not teach or suggest a method for assessing the effectiveness of amprenavir therapy as recited by Claim 80.

Moreover, whether or not mutations at codon 88 inherently affect amprenavir resistance is irrelevant to the novelty of the methods recited by, for example, Claim 80. Applicants are not claiming compositions comprising the particular mutations; instead, Applicants are claiming methods for assessing the effectiveness of therapy with protease inhibitors by detecting the presence of the mutations based upon Applicants' discovery of the correlation between genotype and phenotype. For example, Applicants have discovered that the effectiveness of amprenavir therapy can be assessed by detecting a mutation at codon 88. To successfully assess the effectiveness of amprenavir therapy according to the method of Claim 80, the practitioner must know the relationship between the genotype of HIV protease, *e.g.*, an HIV protease that comprises a mutation at codon 88, and the phenotype of such mutants, *e.g.*, susceptibility to amprenavir. Because *Patick* does not teach this relationship between phenotype and genotype, *Patick* cannot anticipate the methods of the invention, irrespective of the inherent effects of mutations at codon 88 on amprenavir susceptibility.

Further, Applicants note that *Patick* does not teach or suggest the correlation between the presence any of the specific combinations of mutations recited by Claims 83, 86, and 89 and susceptibility to the protease inhibitors recited. *Patick* reports that certain multiple mutants of HIV protease and that such mutants are resistant to nelfinavir. However, as noted above, *Patick* concludes that nelfinavir resistance of such multiple mutants is entirely the result of the mutation at codon 30, which is not recited by any of Claims 83, 86, or 89. Further, *Patick* concludes that none of the mutations recited by the claims affect susceptibility to other protease inhibitors, including amprenavir and indinavir. Thus, *Patick* does not teach the methods recited by Claims 83, 86, and 89.

Finally, *Patick* does not enable one of skill in the art to practice the claimed methods because *Patick* teaches that mutations in the recited codons do not affect resistance to protease inhibitors. Upon reading *Patick*, one of skill in the art would not be able to assess the effectiveness of amprenavir therapy as recited by the methods of Claim 80, 83, 86, and 89

because *Patick* teaches that mutations in the recited codons do not affect amprenavir resistance. *See Patick* at page 2640, last sentence of the paragraph bridging the two columns and second sentence of subsequent paragraph, and at page 2642, first column, second and third full paragraphs. Thus, one of skill in the art would conclude from *Patick* that mutations in codons other than codon 30 are not correlated with protease inhibitor resistance. Without appreciating this correlation, the skilled artisan cannot practice the claimed methods. Therefore, *Patick* does not enable one of skill in the art to practice the claimed methods, and thus cannot anticipate any of Claims 80-91.

In view of the foregoing, Applicants respectfully submit that none of new Claims 80-91 are anticipated by *Patick*, since each of Claims 80, 83, 86, and 89 are novel over *Patick* as shown above, and each of Claims 81, 82, 84, 85, 87, 88, 90, and 91 depend from one of these novel claims. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(a).

CONCLUSION

In light of the above amendments and remarks, Applicants respectfully submit that Claims 80-91 satisfy all the criteria for patentability and are in condition for allowance. Accordingly, Applicants respectfully request that the Examiner reconsider this application with a view towards allowance and solicit an expeditious passage of Claims 80-91 to issuance. The Examiner is invited to call the undersigned attorney at (212) 790-9090, if a telephone call could help resolve any remaining items.

Pursuant to 37 CFR § 1.136(a)(3), the Commissioner is authorized to charge all required fees, fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds LLP U.S. Deposit Account No. 16-1150 (order no. 011068-0035-999).

Respectfully submitted,

Date: November 5, 2003

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